REMARKS

Claims 1-18, 22-25, 27 and 28 were pending as of the issuance of the Office Action of June 22, 2006. Claims 1-18, 22-25, 27 and 28 stand rejected.

Objection to the Title

The title is objected to as "not descriptive." Applicants have amended the title as set forth in the foregoing Amendments to the Specification, thereby rendering the foregoing rejection moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of the foregoing objection.

Priority

Applicants note that a certified copy of the foreign Great Britain patent application will be filed shortly and certainly prior to the issuance of a patent based on the above-identified patent application.

Rejection of Claims 1-18, 22-25, 27 and 28 under 35 U.S.C. § 103(a)

Claims 1-18, 22-25, 27 and 28 have been rejected as being unpatentable over Dumont *et al.* (USPN 6,413,974) (hereinafter referred to as "the '974 patent") in view of Dumont *et al.* (USPN 6,399,633) (hereinafter referred to as "the '633 patent") and Carlson *et al.* (*Cancer Res.* (1999) 59:4634-4641) (hereinafter referred to as "Carlson") on the ground that

> At the time of invention for one ordinarily skilled in the art to use the teachings of Dumont *et al.* (US 6,399,633) that 4-H-1-benzopyran4-one derivatives are suitable for controlling tumor growth... and utilize (R)-roscovitine, taught by Dumont *et al.* (US 6,413,974), a selective and a more potent cyclin dependent kinase inhibitor to study its effects on serine 780 Rb phosphorylation of Rb and levels of phosphorylated ERK1 and ERK2 using the specific antibodies for pRB and ERK1/2.

Applicants respectfully disagree. Applicants submit that the present invention is directed, in part, to a method of monitoring the activity of roscovitine by detecting the presence of phosphorylated erk1 and/or erk2. The present invention is predicated, at least in part, on the identification that roscovitine uniquely induces the phosphorylation of erk1 and/or erk2. Indeed, as

taught by the specification, this property is unique to roscovitine in contrast to related potent cyclin dependent kinase inhibitors (CDKI's), such as purvalanol A which fails to induce the phosphorylation of erk1 or erk2. Furthermore, the CDKI's alsterpaullone and flavopiridol had no effect upon ERK. As such, the detection of phosphorylated erk1 and erk2 can serve as a marker for the monitoring roscovitine activity (see page 2, lines 4-16, page 10, line 3 to page 11, line 23 and Figure 3).

Applicants submit that in order to establish a *prima facie* case of obviousness, it is necessary for the Examiner to present evidence, preferably in the form of some teaching, suggestion, incentive or inference in the applied references, or in the form of generally available knowledge, that one having ordinary skill in the art would have been motivated to make the claimed invention and would have had a reasonable expectation of success in making the claimed invention (M.P.E.P. § 2143). Applying this standard to the references cited by the Examiner, it is clear that a skilled artisan would not have had a reasonable expectation of success in arriving at the claimed invention upon review of the cited references at the time of the invention. Indeed, while USPN 6,399,633 teaches the assessment of phoshphorylated erk1 or erk2 upon exposure to flavopiridol, the '633 patent actually concludes that flavopiridol has no effect on erk1 and erk2 phosphorylation, and on MAP kinase phosphorylation in general (see column 10, lines 24-55 and column 13, lines 27-30), a conclusion that is similarly set forth in the specification of the present application (see page 2, lines 4-16, page 10, line 3 to page 11, line 23 and Figure 3). Accordingly, one skilled in the art, upon review of the teachings of the '633 patent would not seek to identify the effect of other CDKI's on the phosphorylation of erk1 and erk2. Indeed, upon review of the '633 patent, one skilled in the art would reasonably expect that other CDKI's act in a similar manner as flavopiridol and thus, do *not* induce the phosphorylation of erk1 and erk2. To arrive at the claimed invention, a skilled artisan would actually have to dismiss the conclusions of the '633 patent. Accordingly, Applicants submit one skilled in the art would not have a reasonable expectation of success in arriving at the claimed invention.

Applicants further submit that the '974 patent and Carlson fail to account for the deficiencies of the '633 patent in this regard. Indeed, the '974 patent and Carlson each fail to provide a skilled artisan a reasonable expectation of success in arriving at the claimed invention, *i.e.*, these references

fail to provide a skilled artisan an expectation that roscovitine would induce the phosphorylation of erk1 and/or erk2 where a compound of the same class has no such effect. Indeed, neither the '974 patent nor Carlson even discuss CDKI's in the context of erk1 and erk2.

Accordingly, because a skilled artisan would not have had a reasonable expectation of success in arriving at the claimed invention at the time of the invention, Applicants submit that the claimed invention is nonobvious over the cited references and respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

Applicants believe that no additional fee is due with this submission. However, if the Applicants are in error, the Commissioner is authorized to charge any deficiency in the fees paid herewith, or credit any overpayment, to Deposit Account No. 12-0080, under Order No. CCI-026US, from which the undersigned is authorized to withdraw.

If there are any remaining issues or if the Examiner believes that a telephone conversation with Applicants' Attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By _____

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